Please Cancel Claim 26:

26. (CANCEL) The method of claim 25 wherein in step (a) the at least one autoantigen is at least one of human DNA-PK_{cs}, human PARP and human NuMA, and step (b) comprises contacting said at least one human autoantigen with granzyme B.

REMARKS

Upon entry of this Amendment, Claims 23-25, 27 and 30 will be pending in this application.

Amendment of the Specification

Applicant amends the specification to insert SEQ ID NOs as requested. Applicant amends Tables 2 and 3 by providing substitute pages. SEQ ID NOs have been inserted into new columns in each table. In view of the present amendments, Applicant requests withdrawal of the objections to the specification.

Amendment of the Claims

Applicant cancels Claim 26 without prejudice to reintroduction of the claim in a further application.

Claim 23 is amended to more particularly claim the method of generating human autoantigens from human DNA-PK_{cs} and human NuMA.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejected Claims 23-27 as anticipated by Froelich et al, citation 23 on the IDS submitted 2-14-00. As described in Applicant's response of September 26, 2001, Applicant respectfully disagrees. Applicant reiterates Applicant's belief that the stated rejection does not state a proper case of anticipation of the claims.

However, Applicant has presently amended the claims to separate the general method, and the recitation of human PARP from the method of generating human autoantigenic

fragments from human DNA-PK_{CS} and human NuMA. Applicant reserves the right to introduce claims to the separated subject matter in a further application.

In view of the present amendments, Applicant requests that the stated rejection be withdrawn.

Rejection under 35 U.S.C. § 112, 1st paragraph

The Examiner rejected all the claims stating that Applicant has "no support for the subgenus human." Applicant respectfully traverses.

The Examiner is referred to the specification in general and to page 11 in particular. At page 11 a "patient" is defined as particularly "human." An "autoimmune condition" is defined in reference to the immune system of a "patient." Immediately thereafter "autoantigen" and "autoantigenic fragment" are defined with respect to their interaction with said immune system. The Examiner is also referred to lines 18 –35 of page 13 where "autoantigenic fragments" are described in reference to a patient (particularly page 13, lines 29 and 35).

Moreover, the Examiner is directed to FIGS 9A, 10A and 11A wherein it is described that the NuMA and DNA- PK_{CS} shown are "human."

Therefore, Applicant believes there is sufficient support for the subgenus "human" and respectfully requests withdrawal of the stated rejection.

Telephone Conference

Applicant invites the Examiner to contact Applicant's undersigned attorney to discuss the claims if such discussion could further the prosecution of this application.

CONDITIONAL PETITION

Applicant hereby makes a Conditional Petition for any relief available to correct any defect in connection with this filing, or any defect remaining in this application after this filing. The Commissioner is authorized to charge deposit account 13-2755 for the petition fee and any other fee(s) required to effect this Conditional Petition.

CONCLUSION

In view of the foregoing remarks, it is believed that the grounds of the rejections have been addressed and that Claims 23-25, 27 and 30 are in condition for allowance.

Respectfully submitted,

By _____

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Date: Nov. 08, 2002

VERSION OF AMENDED CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

23. (Twice Amended) A method of making [an] at least one human autoantigenic fragment from [an] at least one human autoantigen selected from the group consisting of human DNA-PK_{cs} and human NuMA, comprising the steps of

(a) isolating cells containing at least one human autoantigen, and

(b) contacting the cells with a lymphocyte granule enzyme to produce a mixture containing at least one human autoantigenic fragment.

26. (CANCEL) The method of claim 25 wherein in step (a) the at least one autoantigen is at least one of human DNA-PK_{cs}, human PARP and human NuMA, and step (b) comprises contacting said at least one human autoantigen with granzyme B.

Table II: Different fragments are detected after *in vitro* cleavage of autoantigens with granzyme B versus caspase-3.

The data obtained in FUG. 2, using purified DNA-PK_{cs}, [^{35}S]methionine labeled PARP, endogenous DNA-PK_{cs} and NuMA, and purified proteases, were used for the tabulation below.

Substrate	Fragments induced after cleavage with Granzyme B	Caspase-3	Likely granzyme B Cleavage sites	Of SEQ ID No.
DNA-PK_{cs}2	100kDa	150kDa	$VDQD^{3210}$-G^{3211}	34
DNA-PK_{cs}3	250kDa	250kDa	$VGPD^{2698}$-F^{2699}; $DEVD^{2712}$-N^{2713}	34 34
NuMA	175kDa	185kDa	$VLGD^{411}$-V^{412}	32
PARP	62kDa	89kDa	$VGPD^{537}$-S^{538} (Froelich *et al.*, 1996a)	33

2 DNA-PK_{cs} fragments were detected by immunoblotting with monoclonal antibody 25-4 or patient sera A.G. and G.A. (which all recognize the C-terminuis).

3 DNA-PK_{cs} fragments were detected by monoclonal antibody 18-2 (which recognizes the N-terminus).

TABLE 3: AUTOANTIGENS ARE EFFICIENTLY CLEAVED BY GRANZYME B

	Autoantigen	Cleavage Site	k_{cat}/K_m($M^{-1}.s^{-1}$)	Fragments (kDa)
1	DNA-PKcs	VGPD^{2698}-F	$2.5 \pm 0.8 \times 10^6$	160, 100
2	Topoisomerase I	I EDA^{15}-f	$1.6 \pm 0.6 \times 10^6$	97,72
3	NuMA	VATD^{1705}-A	$5.4 \pm 1.4 \times 10^5$	175
4	Mi-2	V DPD^{1312}-Y	$8.5 \pm 1.9 \times 10^4$	75, 72, 48
5	La	LEED^{220}-A	$6.1 \pm 1.7 \times 10^4$	21, 28
6	PMS1	LTPD^{313}-K ISA D^{496}-E	$6.9 \pm 0.9 \times 10^4$	48
7	Fibrilliarin	VGPD^{184}-G	$3.3 \pm 1.9 \times 10^4$	20, 17
8	PARP	VDPD^{536}-S	$2.3 \pm 1.8 \times 10^4$	72, 62, 55
9	U1-70kDa	LGND^{409}-S	$1.3 \pm 0.4 \times 10^4$	60
10	PMS2	VEKD^{493}-S	$1.4 \pm 0.6 \times 10^4$	60, 45, 35
11	Isoleucyl tRNA synthetase (O.J.)	VTPD982-Q	$7.8 \pm 1.8 \times 10^4$	
12	Histidyl tRNA synthetase (Jo-1)	LGPD^{48}-E	$2.3 \pm 0.7 \times 10^4$	40
13	Alanyl tRNA synthetase (PL-12)	VAPD^{632}-R	1.8×10^4	63, 40
14	RNA polymerase I	ICPD^{448}-M	$1.3 \pm 0.5 \times 10^4$	140
15	KI-67	VCTD^{1481}-K	$8.1 \pm 2.6 \times 10^3$	168, 148
16	PmScl	VEQD^{252}-M	$7.5 \pm 1.4 \times 10^3$	85, 74, 60
17	CENP B	VDSD^{457}-E	$5.9 \pm 0.2 \times 10^3$	58, 40
18	RNA polymerase II	I TPD^{370}-P	ND	200
19	SRP 72	VTPD^{573}-P	ND	62
20	Ku 70	I SSD^{79}-R	ND	65
21	Tyrosinase	ICTD^{249}		
22	E4	VDVD^{123}		
23	Golgin 160	SEVD^{311}		
23	Golgin 160	VGPD^{92}		
2	Golgin 160	IEAD^{648}		
	Myosin			